# Characterization of yeast genes homologous to human genes involved in mitochondrial and peroxisomal function

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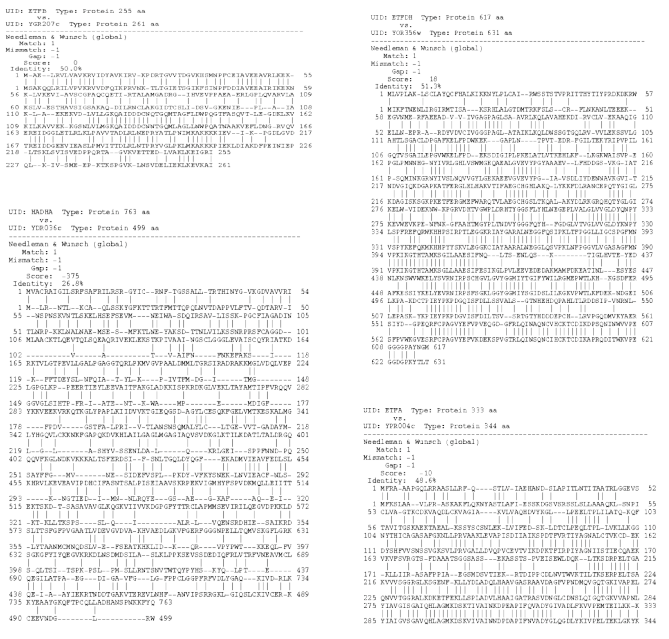
The *Saccharomyces cerevisiae* genes *YPR004c*, *YGR207c*, *YOR356w* and *YDR036c* homologous to human genes involved in transfer of electrons to the respiratory chain from flavin-containing dehydrogenases (ETFA, ETFB and ETFDH) and in β-oxidation (HADHA), were chosen for characterization. Mutations in ETFA, ETFB and ETFDH (orthologous to *YPR004c*, *YGR207c* and *YOR356w*, respectively) cause multiple acyl-CoA dehydrogenation deficiency, also known as glutaric aciduria II. Mutations in HADHA (orthologous to *YDR036c*) affect the α-subunit of the trifunctional enzyme that catalyzes three reactions in mitochondrial β-oxidation of fatty acids. In previous studies, all of these yeast genes have been localized in the mitochondrion. Unlike mammalian cells, fatty acid catabolism by β-oxidation in yeast takes place exclusively in peroxisomes. The aim of this work is to contribute to understand the functional relation between mitochondria and peroxisomes, by studying lipid catabolism in yeast cells. *S. cerevisiae* mutants affected in the above mentioned genes were studied for growth on several non-fermentable carbon sources and for carbon sources, which catabolism requires peroxisomal activity (oleic acid and methanol). Growth is unaffected on non-fermentable carbon sources and is decreased for all mutants only on methanol, which suggests deficiency in peroxisomal activity concomitant with normal function of mitochondria. On the other hand, *ygr207c* and *yor356w* mutant strains present growth deficiency on oleic acid, suggesting a wider peroxisomal metabolic deficiency when compared to *ypr004c* and *ydr036c*.

## Yeast genes studied, human orthologues and related diseases

| Yeast gene | Human orthologue | Human disease |
|---|---|---|
| *YPR004c* | ETFA | Glutaric aciduria type IIa |
| *YGR207c* | ETFB | Glutaric aciduria type IIb |
| *YOR356w* | ETFDH | Glutaric aciduria type IIc |
| *YDR036c* | HADHA | Trifunctional enzyme deficiency |

## Human and yeast genes sequence homologies




## Potential transcriptional regulators#

| Gene | Sequences | Transcription factors |
|---|---|---|
| *YPR004c* | TTGGGG( -826) TTGGAG (-900) | Adr1p |
| | GGTAC ( -129, -735) GTCAC ( -153, -382) | Rtg1p |
| *YGR207c* | TTGGAG ( -704) | Adr1p |
| | GGTAC ( -374) GTCAC ( -743) | Rtg1p |
| *YOR356w* | TTGGAG ( -772, -948) TTGGGG ( -990) | Adr1p |
| *YDR036c* | TTGGAG ( -423) | Adr1p |
| | GTCAC ( -445) | Rtg1p |

**Rtg1p**

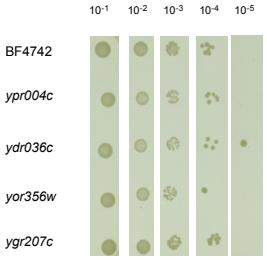
Positive transcriptional regulator controlling expression of *ADH2*, peroxisomal protein genes and genes involved in ethanol, glycerol and fatty acid utilization.

**Adr1p**

Transcription factor involved in interorganelle communication between mitochondria, peroxisomes and nucleus.

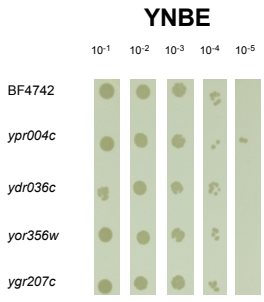
# Yeast Search for Transcriptional Regulators And Consensus Tracking (YEASTRACT), [November 28, 2005]

## All strains grow on glucose



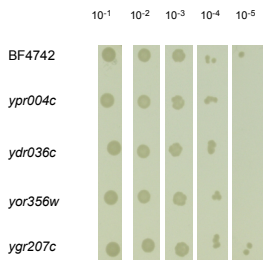

0,67% Yeast Nitrogen Base with amino acids; 0,1% Yeast extract; 2% Agar and 2% Dextrose

## All strains grow on ethanol



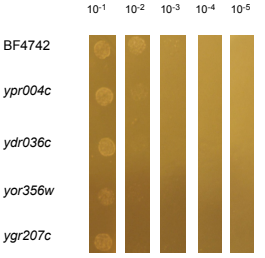

0,67% Yeast Nitrogen Base with amino acids; 0,1% Yeast extract; 2% Agar and 2% Ethanol

## All strains grow on glycerol



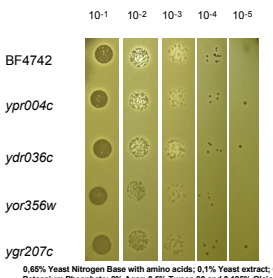

0,65% Yeast Nitrogen Base with amino acids; 0,1% Yeast extract; 2% Agar and 2% Glycerol

## All mutant strains have growth deficiency on methanol




0,65% Yeast Nitrogen Base with amino acids; 0,1% Yeast extract; 0,5% Potassium Phosphate; 2% Agar and 2% Methanol

## Mutant strains *yor356w* and *ygr207c* have growth deficiency on oleic acid




0,65% Yeast Nitrogen Base with amino acids; 0,1% Yeast extract; 0,5% Potassium Phosphate; 2% Agar; 0,5% Tween 80 and 0,125% Oleic Acid